REMARKS AND ELECTION OF CLAIMS

Claims 1–49 were under consideration in the outstanding Office Action. Claims 34-42 have been canceled by the amendment presented above without disclaimer of any subject matter. Claims 50 and 51 have been added.

New Claim 50 is similar to claim 32, except that claim 50 recites a method of evaluating Factor IX_a activity rather than $FVIII_a$ activity. This claim language is supported by the specification at page 22, lines 4-7.

New claim 51 is similar to original claim 33 except that new claim 50 depends from base claim 49 rather than claim 32.

Accordingly, Applicants submit that claims 50 and 51 find support in the application as filed, and respectfully request their entry and consideration.

The Office Action states that the claims are directed to ten inventions that are not so linked as to form a single general inventive concept under PCT Rule 13.1, and that Applicants are required to elect a single invention to which the claims must be restricted. Specifically, the Office Action states that "[t]he shared technical feature of the main invention (Groups I and IX) is the combination of a soluble phospholipid and a reagent (i.e. contact activator, soluble tissue factor, or composition comprising Factor X), wherein said sample comprises an incubated blood/plasma mixture, which is shown by Triplett (US 5,705,198) to not make a contribution over the prior art." The Office Action further alleges that "Triplett teaches a clotting activity method comprising combining a plasma sample, soluble phospholipid, and contact activator, and calcium (chloride) including the incubation thereof to activate thrombin/detect thrombin activity (abstract; summary; column 5, para. 4; examples 4 and 5)."

Applicants respectfully disagree with this characterization of the present invention and the Triplett patent. The common technical feature of the present claims is a soluble phospholipid, which provides a novel and nonobvious contribution over the art. Thus, the claims embody a special technical feature that unifies the claims, and the present restriction should be reconsidered and withdrawn.

Applicants respectfully point out that the Triplett patent does not disclose a soluble phospholipid. As described in the present specification at page 13 (lines 27-28) a soluble phospholipid "comprises essentially no aggregates (*e.g.*, as lamellar or non-lamellar structures)." In contrast, Triplett et al. only discloses use of

conventional, insoluble (*i.e.*, aggregated, solid-phase) phospholipids that are prepared from natural sources.

For example, at page 4 (lines 23-25), Triplett et al. states that "[a] clotting test, sensitive to LA can be carried out by mixing a plasma sample with a suitable amount of a phospholipid suspension . . .." (*emphasis added*) Applicants respectfully note that a "suspension" is a solid phase dispersed in a fluid. Thus, the "phospholipid suspension" of Triplett et al. is insoluble.

Further, at Col. 5 (lines 25-32), Triplett et al. teaches that:

> Phospholipids suitable for the performance of the PLDPA tests are preparations containing phosphatidylethanolamine (Synonym: colamine kephalin) and phosphatidylserine (Synonym: serine kephalin) which are obtainable from animal, plant or microbial biomass by organic solvent extraction. Suitable phospholipid preparations e.g. from bovine brain, egg yolk or soy bean are commercially available from Sigma Chemical Company, St. Louis, Mo., USA.

In addition, the Examples of the Triplett et al. patent use phospholipids prepared from rabbit brain.

It is well-established in the art that phospholipids isolated from natural products such as animal, plant or microbial sources, are insoluble[1]. In particular, these phospholipids from natural products have fatty acids that are generally C16 or longer[2], and which spontaneously form micelles or other membrane-like structures[3]. This property is not surprising as the source of phospholipids in natural products is primarily from cellular membranes. Phospholipid preparations isolated from natural sources are commonly referred to as "synthetic membranes." Synthetic membrane

---

[1] *See, e.g.*, Bloor, W.R. Biochemistry of the fats. *Chem. Rev.* 2: 243-300 (1925).

[2] *See, e.g.*, Tables 28-4 and 28-5 from Marcus, A.J., Chapter 28 "Multicellular Eicosanoid and Other Metabolic Interactions of Platelets and Other Cells" *in* Hemostasis and Thrombosis: Basic Principles and Clinical Practice, Vol 3, 1994, JB Lippincott, Philadelphia, PA (*copy enclosed*). *See also*, page 97 of Tanford, C., Chapter 12 "Biological Lipids" *in* The Hydrophobic Effect: Formation of Micelles and Biological Membranes, 1973, John Wiley & Sons, New York, NY (*copy enclosed*).

[3] *See, e.g.*, Tanford, C., Chapter 12 "Biological Lipids" *in* The Hydrophobic Effect: Formation of Micelles and Biological Membranes, 1973, John Wiley & Sons, New York, NY (*copy enclosed*), for example, the discussion at page 98 (second para) and at pages 99-100 ("Critical Micelle Concentration").

preparations are conventional in the art and are discussed in the present specification at page 13, lines 4-9 and 15-18[4].

Thus, Triplett et al. only teaches the use of insoluble phospholipid preparations and does not disclose or suggest using the soluble phospholipids of the present invention, which provide a special technical feature and unify the claims. Accordingly, it is respectfully requested that the outstanding Restriction Requirement be withdrawn.

Nonetheless, as a complete response to the Restriction requires an election, Applicants elect the claims of Group I (claims 1-15 and new claim 51, drawn to a method of evaluating clotting activity) with traverse for the reasons set forth above.

This application is now in condition for substantive examination, which action is respectfully requested.

Respectfully submitted,

Karen A. Magri
Registration No. 41,965

Enclosures:
Marcus et al.
Tanford et al.

Customer No. 20792
Myers Bigel Sibley & Sajovec, P.A.
P. O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

CERTIFICATION OF ELECTRONIC TRANSMISSION
I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on July 28, 2008.

Claire Wimberly

[4] *See also,* Okuda et al. Usefulness of synthetic phospholipid in measurement of activated partial thromboplastin time: a new preparation procedure to reduce batch difference. *Clin. Lab. Haematol.* 26: 215-223 (2004).